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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,320	MARTIS ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *10-18 and 26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 19-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9 and 19-25, drawn to a method of manufacturing a peritoneal dialysis system, classified in class 435, subclass 31.

II. Claims 10-18, drawn to a method of providing peritoneal dialysis to a patient, classified in class 604, subclass 29.

III. Claims 26-30, drawn to a glucose polymer composition, classified in class 424, subclass 537.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are distinct inventions and thus are subject to restriction. The inventions are distinct processes in that the methods are not dependent on each other, not to be used together and have different functions, modes of operation, and effects. In the instant case the method of invention I requires the peritoneal dialysis solution to be made with a glucose polymer, which is not required in the dialysis solution used in the method of invention II. Additionally, the method of invention II requires a step of administering the peritoneal dialysis solution to the patient, which is not required in the method of invention I.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of invention III can alternatively be used as a cell broth nutrient medium comprising antibiotics. Antibiotics, such as penicillin G, react with the peptidoglycans by interfering with bacterial cell wall formation (See

"The Prokaryotic Cell: Bacteria"). Therefore, cell broth nutrient medium comprising glucose polymers as the carbon source and an antibiotic, such as a penicillin, is an alternative use for a glucose polymer composition comprising a reagent capable of reacting with a peptidoglycan.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the method of invention II does not require the glucose polymer composition of invention III.

Therefore, a search and examination of all inventions in one patent application would result in an undue burden. These inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, different classifications, and a search for one group does not require a search for another group, restriction for examination purposes as indicated is proper.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of

inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Paula Kelly on 28 April 2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-9 and 19-25. Affirmation of this election must be made by applicant in replying to this Office action. Claims 10-18 and 26-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Traversal is on the grounds that groups I and II cover similar subject matter. Specifically, the novelty of both groups is the use of a reagent in a peritoneal dialysis solution to detect levels of peptidoglycan. However, the argument is not found persuasive because the methods of groups I and II are distinct because they comprise different methodologies. The method of group I requires the use of a glucose polymer, which the method of group II does not; additionally the method of group II requires a step of administering the solution to a patient, which is not required in the method of group I. Also, without the specific disclosure of the "reagent" applicant cannot rely on the inclusion of a reagent to impart a shared novelty to the claims. Particularly in the method of group II the independent claim only requires that a peritoneal dialysis solution utilizes "a reagent" to ensure low level of peptidoglycan; in this broad language the reagent may comprise any chemical or enzyme that is capable of indicating peptidoglycan levels, it does not need to be the same reagent used in the method of invention I.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 19-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's claim 1 and its dependents are directed to a method for manufacturing a peritoneal dialysis solution, comprising providing a glucose polymer; adding a reagent to the glucose polymer wherein the reagent is capable of reacting with a peptidoglycan; determining an amount of the peptidoglycan; and using the glucose polymer to make the peritoneal dialysis solution if it is determined that a sufficiently low level of the peptidoglycan is present.

Similarly applicant's claim 19 and its dependents are directed to a method of testing a peritoneal dialysis solution for presence of a gram positive organism that exceeds a level sufficient to cause peritonitis, comprising adding a reagent to the peritoneal dialysis solution wherein the reagent is capable of reacting with the peptidoglycan to initiate a serine protease cascade; and determining the amount of the peptidoglycan.

The term "reagent" in claims 1 and 19 is regarded as insufficient written description of the composition that is added to the solution, therefore applicant has failed to clearly convey the subject matter that they are claiming. Both claims require use of a reagent that is capable of reacting with peptidoglycans but applicant's specification only teaches the specific plasma fraction isolated from silkworm larvae, taught by Ashida et al (US Patent 4,970,152). Thus while applicant provides description of the silkworm larvae fraction, they fail to provide sufficient written description of a representative number of species of suitable reagents capable of reacting with peptidoglycan, which is required to claim the entire genuses of reagents capable of reacting with peptidoglycan. Such a broad genus would encompass enzymes such as peptidases and glycosyltransferases, which applicant has provided no written description of. Additionally, there is no disclosure of relevant, identifying characteristics, such as

structure or other physical or chemical properties, or functional characteristics, beyond disclosure of the generic action (capable of reacting with peptidoglycan), sufficient to show the applicant was in possession of the claimed genus. *See Eli Lilly,* 119F. 3d. at 1568, 43 USPQ2d at 1406. See MPEP § 2163.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 19-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 1 and its dependents are directed to a method for manufacturing a peritoneal dialysis solution, comprising providing a glucose polymer; adding a reagent to the glucose polymer wherein the reagent is capable of reacting with a peptidoglycan; determining an amount of the peptidoglycan; and using the glucose polymer to make the peritoneal dialysis solution if it is determined that a sufficiently low level of the peptidoglycan is present.

The step comprising "determining an amount of the peptidoglycan" is unclear. It appears applicant intends to require determination of the amount of peptidoglycan in the glucose polymer; however, as stated it is not clear if the peptidoglycan is to be present in the glucose polymer, and if so, it is not clear if applicant is requiring a certain amount of peptidoglycan to be present, and if so, how much. Additionally, it is claimed that if a sufficiently low level of peptidoglycan is present the glucose polymer is to be used to make the peritoneal dialysis solution. Again, it is not clear from the claim language if reference is being made to the peptidoglycan level in the glucose polymer or peptidoglycan level elsewhere.

Still further, it is not clear what the reagent consists of. It is not clear if any reagent that is capable of reacting with a peptidoglycan, such as a peptidase, is encompassed by the claimed invention.

Still further, the term "sufficiently low level" (of peptidoglycan) is indefinite because no standard can be ascertained for the acceptable level of peptidoglycan or what is a "sufficiently" low level of peptidoglycan; thus the metes and bounds of the claims cannot be determined.

Finally, it is not clear what one does if the peptidoglycan level is not "sufficiently low." The claim has no utility if the peptidoglycan level is not "sufficiently low," as the solution then cannot be used to make the peritoneal dialysis solution. Rather it appears a positive step is required to reduce the peptidoglycan level if it is not "sufficiently low."

Applicant's claim 5 requires the amount of peptidoglycan to be further determined by a colorimetric measurement in response to the reaction between the peptidoglycan and the reagent. It is not clear if this determination step is subsequent to an initial determination step ("further determined by"), if so, it is not clear how the peptidoglycan level is initially determined.

Applicant's claim 7 requires the reagent to be added to the peritoneal dialysis solution. It is unclear how the reagent is added to the peritoneal dialysis solution when claim 1 requires the reagent to be part of the peritoneal dialysis solution. Claim 1 requires the reagent to be added to the glucose polymer; thus it appears claim 7 intends to require the reagent to be added to the glucose polymer, which fails to further limit claim 1. Additionally, the term "reagent" is unclear as it is uncertain if applicant intends to claim any reagent capable of reacting with peptidoglycans.

Applicant's claim 8 requires the method of claim 1 to further comprise a step of removing the peptidoglycan to provide the sufficiently low level of same if it is determined that the sufficiently low level of the peptidoglycan is not present. It is not clear what is intended by the term "to provide the sufficiently low level of same." If, in fact, in claim 1 the peptidoglycan level is "sufficiently low" this

step has no utility. It appears this step needs to be incorporated into claim 1 to ensure a "sufficiently low level of peptidoglycan." Additionally, it is not clear how the excess peptidoglycan is removed.

Applicant's claim 19 and its dependents are directed to a method of testing a peritoneal dialysis solution for presence of a gram positive organism that exceeds a level sufficient to cause peritonitis, comprising adding a reagent to the peritoneal dialysis solution wherein the reagent is capable of reacting with the peptidoglycan to initiate a serine protease cascade; and determining the amount of the peptidoglycan.

The term "sufficient" is indefinite because no standard can be ascertained for the sufficient level to cause peritonitis; thus the metes and bounds of the claims cannot be determined.

Also, in both claims 19 and 24, it is not clear what the reagent consists of. It is not clear if any reagent that is capable of reacting with a peptidoglycan, such as a peptidase, is encompassed by the claimed invention.

The term "the peptidoglycan" is recited in the fifth line of the claim; there is insufficient antecedent basis for this limitation.

Finally, it is not clear if the peptidoglycan is in the peritoneal dialysis solution.

Applicant's claim 24 requires the reagent to be added to the glucose polymer in a 'raw material form.' It is not clear what raw material form the reagent is to come in, as it is unclear what the reagent is.

Applicant's claim 25 requires the glucose polymer-based solution to be tested fro the amount of peptidoglycan that exceeds about 10 ng/mL. It is not clear if 10 ng/mL is the level sufficient to cause peritonitis. Additionally, the antecedent basis for the limitation "the amount" in the second line of this claim is unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 and 19-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gokal et al (Perit Dial Int, 2002), Martin et al (Advances in Peritoneal Dialysis, 2003) and Goffin et al (Nephrol Dial Transplant, 2003), each in view of Tsuchiya et al (FEMS, 1996), further in view of Ashida et al (US Patent 4,970,152).

Gokal et al describe icodextrin as the colloid osmotic agent in peritoneal dialysates, commercially available as EXTRANEAL. At the time of the article use of icodextrin peritoneal dialysates was associated with an increased rate of sterile peritonitis. Gokal et al report that testing by the manufacturer revealed the icodextrin solutions were contaminated with peptidoglycan, a non-endotoxin, weak pyrogen contained in the cell wall of gram positive bacteria and fungi (See Gokal et al, pg. 447-448). Gokal et al report the manufacturer performed silkworm larvae plasma tests to identify peptidoglycan as the contaminant.

Similar reports by Martin et al and Goffin et al teach manufacturer reported that the increased frequency of sterile peritonitis in peritoneal dialysis patients using icodextrin-containing dialysates was due to peptidoglycan contamination in certain batches of icodextrin-containing dialysates (See Goffin et al, Pg. 2483 & Martin et al, Pg. 193).

The silkworm larvae plasma test (SLP test) is used to detect peptidoglycans using the prophenol oxidase cascade; it can be used to detect microbial contamination. Silkworm larvae plasma contains all the factors of the prophenol oxidase cascade; when added to a sample suspected of containing peptidoglycan the peptidoglycan activates the prophenol oxidase cascade resulting in the production of melanin, which can be colorimetrically measured (See Tsuchiya et al, Pg. 131-134).

Therefore, Gokal et al disclose the use of the SLP test which involves addition of a silkworm larvae plasma reagent (which applicant calls a reagent in its raw material form) to an icodextrin-containing dialysate solution to test for the presence of peptidoglycan, which is indicative of gram positive bacteria contamination in the icodextrin-containing dialysate (Claims 7 and 19-24).

Though Gokal et al teach performing the SLP test on batches of peritoneal dialysis solution, and not the raw icodextrin, it would have been obvious to one of ordinary skill in the art at the time the invention was made to test the icodextrin before formulation of the complete peritoneal dialysis solution. One of ordinary skill in the art would have been motivated to test the raw icodextrin for peptidoglycan contamination before mixing the complete dialysis solution in order to reduce waste. For example, if the icodextrin was found to be contaminated, the tester would discard only the icodextrin, as opposed to formulating the complete dialysis solution, which comprises additional electrolytes and chemicals, then testing to find out the icodextrin was contaminated and having to discard the entire solution, thus wasting the additional electrolytes and chemicals. One would expect success testing a solution of pure icodextrin because the SLP test responds to the presence of peptidoglycan; it does not require additional reagents present in a complete dialysate.

Additionally, though Gokal et al do not report the concentration of peptidoglycan found in the contaminated icodextrin nor do they report an acceptable threshold level of peptidoglycan that can be tolerated in the peritoneal dialysate solution, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the concentration of peptidoglycan in peritoneal dialysis solution, and furthermore to remove excess peptidoglycan to obtain an acceptably low level for administration (Claims 1-6, 8-9 and 25). Because the SLP test produces melanin as an end product it would have been obvious to one of ordinary skill in the art to perform colorimetric measurements to determine the amount of peptidoglycan in the solution. Ashida et al teach a method to correlate melanin production to peptidoglycan concentration by creating a standard curve using known amounts of

peptidoglycan, and then comparing the experimentally obtained measurements (See Ashida et al, col. 12, ln 10-52). One of ordinary skill in the art would have been motivated to determine the concentration of peptidoglycan present in contaminated samples of icodextrin in order to determine if the level is acceptably low enough for safe distribution or if peptidoglycan must be removed through methods known in the art, such as affinity or ligand chromatography or enzyme degradation (See, e.g. Ashida et al, col. 5, ln 20-29). One would have expected success quantifying the concentration of peptidoglycan in the solution and then altering the concentration to an acceptable level because Ashida et al teach methods of colorimetrically determining the amount of peptidoglycan present in a sample and that peptidoglycan can be digested by enzymes such as egg white lysozyme.

Finally, though there are no teachings on the specific concentrations of peptidoglycans which are tolerable in peritoneal dialysis solutions, the reports by Gokal et al, Martin et al and Goffin et al show that only a percentage of the people treated with the contaminated icodextrin solutions experienced sterile peritonitis and symptoms varied within the results; the references also teach that it is possible for patients to have allergic responses to the contaminated icodextrin. Therefore, it is clear that the tolerably level of peptidoglycan varies based on the individual; size, dosage requirements, and allergies effect how an individual patient tolerates peptidoglycan. However, in general the level of peptidoglycan in the peritoneal dialysis solution is a result effective variable, and thus the proportions and amount of peptidoglycan deemed acceptable in the solution would be routinely optimized by one of ordinary skill in the art. One of ordinary skill in the art would be able to manipulate the acceptable level of peptidoglycan based on a person's individual response to peptidoglycans. Therefore, one may begin using peritoneal dialysis solution with a peptidoglycan level of 10 ng/mL or less, however, through routine experimentation one may find the individual's tolerance to require a level of much greater purity, or one may find the individual can tolerate much higher levels of peptidoglycans with no adverse effects. One would be motivated to perform routine experimentation to determine an individual's tolerance level of

peptidoglycan in order reduce costs, for the individual, associated with peptidoglycan removal, as clearly there is a cost associated with purification of peritoneal dialysis solutions, increased purity would be associated with higher costs.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER